

Application No.: 10/582,056
Filing Date: January 29, 2007

AMENDMENTS TO THE DRAWINGS

Please replace the drawings with the Replacement Sheets provided herewith.

REMARKS

Claims 1 and 3-10 are presently pending. The limitation of canceled Claim 2 is incorporated in to Claim 1. Support for other amendments to the claims is discussed below. Claims 11-23 are canceled without prejudice. No new matter has been added herewith. The following addresses the substance of the Office Action.

Objections to the Drawings

The Drawings were objected to because they had a Chinese character before the Arabic figure number. Replacement sheets provided herewith delete the Chinese character and substitute the word "Fig."

Indefiniteness

Claims 1-19 and 21-23 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

Claim 1 was found to be confusing because it referred to plural "lymphocytes" in the preamble and in steps 1) and 2), but it referred to a singular "lymphocyte" in steps 3) and 4. Applicants have amended Claim 1 to consistently recite "lymphocytes."

Claim 1 was found to be unclear because it did not set forth the differences in components added to test wells and control wells. Applicants have amended Claim 1 to distinguish between test and control lymphocytes. Test lymphocytes are exposed to a target antigen, whereas control lymphocytes are exposed to either irrelevant antigen or no antigen. Support for the amendments is found in the Specification as filed, for example at page 5, lines 18-22 and at page 21, lines 8-9 and 12-13.

Claim 1 was also found to be unclear because it did not state how the "comparing" of step 4 relates to the purpose of "detecting specificity of activated lymphocytes set forth in the preamble. Applicants have amended the preamble to recite --A method for detecting antigen-specific, activated lymphocytes--. Moreover, in accordance with the Examiner's suggestion, the Applicants have added the limitation --wherein a lower activity of the test lymphocytes compared to the control lymphocytes is indicative of antigen-specific activated lymphocytes in the organism--. Support for the amendment is found in the Specification as filed, for example at page 16, lines 4-6.

Claim 1 was also rejected as being indefinite for omitting essential functional cooperative relationships of elements. In particular, the claim did not explain how the “incubating” of step 3) gave rise to any “detectable signals” that were to be compared in step 4). Applicants have amended Claim 1 by simplifying the claim language. Amended Claim 1 recites -- determining activity in said test lymphocytes and in control lymphocytes from said organism by measuring a detectable signal --. Claim 5 is amended to recite that the detectable signal is measured by a method selected from the group consisting of MTT colorimetry, cell staining, fluorescent antigen staining and enzyme linked immunosorbent assay. Support for the amendments is found in the Specification as filed, for example at page 16 (line 26)- page 17 (line 23).

Claim 5 was found to be unclear for reciting “activity changes” while not stating what component used in Claim 1 has any changes in “activity.” As noted above, Claim 1 is amended to recite that activity is determined by measuring a detectable signal, and Claim 5 is amended to recite specific types of detectable signal are measured to determine cell activity.

Claim 10 was found to not have antecedent basis for “the cytokines which can stimulate cell proliferation” since Claim 1 recited “cytokines which can induce cell proliferation.” Applicants have amended Claim 10 to recite -- cytokines which can induce cell proliferation--.

Claim 12 was found to be indefinite for reciting a use without any active, positive steps delimiting how the use is actually practiced. Claim 12 was also found to be unclear for not clearly specifying whether one or more of the listed ingredients must be present in the medium. Claim 12 is canceled, thereby obviating the rejections.

Claim 14 was found to lack antecedent basis for recitation of “the cytokine neutralizing antibody used which can induce cell proliferation” because Claim 12 refers to “neutralizing antibodies against cytokines which can induce cell proliferation.” Claim 14 is canceled, thereby obviating the rejection.

Claim 15 and dependent Claim 23 were found to lack antecedent basis because recitation of “the cytokines which can inhibit mononuclear cell activation” was not supported by Claim 12, which referred to “cytokines which inhibit cell activation or inhibit cell proliferation.” Applicants have canceled Claims 15 and Claim 23, thereby obviating the rejection.

In Claim 18 and dependent Claim 19, recitation of “the anti-cancer medicaments” and/or of “or inducing tumor cell apoptosis” were unclear, because Claim 13 only referred to the

concentration range of “immunosuppressive agents.” Applicants have canceled Claims 18 and 19, thereby rendering the rejection moot.

Claim 22 was found to lack antecedent basis for recitation of “the cytokines which can stimulate cell proliferation” because independent Claim 12 recites “cytokines which can induce cell proliferation.” Applicants have canceled Claim 22, thereby obviating the rejection.

Claims 22 and 23 were found to lack antecedent basis for recitation of “The method.” Applicants have canceled Claims 22 23, thereby obviating the rejections

In view of the amendments to the claims and the preceding remarks, the Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

Written Description

Claim 8 (the Patent Office intended to indicate Claim 6) and Claim 18 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Patent Office found that there is no disclosed representative member of “other medicaments which are potentially capable of inducing immunosuppressive function or inducing tumor cell apoptosis,” which is a large subgenus of medicaments which were not described, except by function. Applicants have canceled recitation of the phrase from Claim 6 and Claim 18 is canceled, thereby obviating the rejection.

Anticipation

Hamawy et al.

Claims 1-5, 11-12, 15 and 23 were rejected under 35 U.S.C. § 102(b) as being anticipated by Hamawy et al. (U.S. Patent No. 6,150,121). Hamawy et al. teaches a method wherein Peripheral Blood Lymphocytes (PBL) isolated from the blood of a graft recipient is exposed to either graft-derived fibroblast-like (GDFL) cells derived from the graft recipient or GDFL cells from a third party (i.e., graft cells derived from a subject other than the donor). Hamawy et al. then measured [³H] thymidine uptake in the presence and absence of IL-2. The object of Hamawy et al. is to provide “a method for diagnosing graft rejection reaction by culturing graft cells as antigens with the lymphocytes in the peripheral blood of the subject” to learn the proliferation of the cells and the increasing of the activity of the cells.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed.Cir. 1986). “[A]nticipation requires that all of the elements and limitations of the claim are found within a single prior art reference.” See *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). The method of Hamawy et al. does not involve neutralizing antibodies against cytokines which can induce cell proliferation and it does not teach or suggest that antigen can inhibit the activity of specifically activated lymphocytes and induce the apoptosis of the specific activated lymphocytes in the presence of the neutralizing antibodies against cytokines which can induce cell proliferation. Accordingly, the present claims are not anticipated by Hamawy et al.

The presently claimed methods are also not obvious in view of Hamawy et al. In contrast to Hamawy et al., the technical problem solved by the present invention lies in detecting the specificity of activated lymphocytes against an antigen. The technical solution used is a combined usage of antigen capable of activating lymphocytes and neutralizing antibodies against cytokines, which can induce cell proliferation. Thus, the Applicants have discovered a method that can inhibit the activity of the specific activated lymphocytes and induce the apoptosis of the specific activated lymphocytes in the presence of the neutralizing antibodies against cytokines which can induce cell proliferation. Those of ordinary skill in the art could not have foreseen the technical solution of Claim 1 based on the teaching of Hamawy et al. Accordingly, the method of Claim 1 is neither anticipated nor obvious in light of Hamawy et al.

Stafford et al.

Claims 12, 14, 16-17 and 22 were rejected under 35 U.S.C. § 102(b) as being anticipated by Stafford et al. (U.S. Patent No. 6,346,247). Stafford et al. teaches a medium that comprises a 2-fold dilution of an avian anti-IL-2 polyclonal antibody, which had a starting concentration in the range of 20-35 mg/ml. Stafford et al. also teaches a medium that comprises various dilutions of an anti-IL-12 polyclonal antibody.

The Applicants have canceled Claims 12, 14, 16-17 and 22, thereby rendering the rejection moot.

Karpas et al.

Claims 12-13, 18-19 and 21 were rejected under 35 U.S.C. § 102(b) as being anticipated by Karpas et al. (U.S. Patent No. 5,801,144). Karpas et al. teaches a medium containing the immunosuppressants CsA or FK506 at concentrations of 1, 4 or 10 µg/ml.

The Applicants have canceled Claims 12-13, 18-19 and 21, thereby rendering the rejection moot.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' amendments to Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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